AMENDMENTS TO THE CLAIMS

Please amend claims 1, 5, 6, 9, 29, 30, 34, 35, 54, 59, and 63, enter new claim 74, and cancel claims 4, 36, 50, 53, and 58, without prejudice, as follows.

1. (Currently amended) A method of decreasing an IFN-γ parameter [[in]] of a subject having an excess of IFN-γ, the method comprising:

(a) evaluating the IFN-γ parameter of [[a]] the subject;

(b) comparing the IFN-γ parameter [[in]] of the subject to the IFN-γ parameter of a normal subject, wherein a substantial increase in the IFN-γ parameter [[in]] of the subject relative to the normal subject indicates that the subject has ~~the~~ an excess of IFN-γ; and

(c) administering to the subject ~~having the excess IFN-γ~~ an agonist of [[an]] interleukin-21 (IL-21)/IL-21 receptor (IL-21R), wherein ~~said~~ the agonist is selected from the group consisting of:

(i) a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2,

(ii) a murine IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:4,

(iii) an agonistic anti-human IL-21R antibody, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:6, and

(iv) an agonistic anti-murine IL-21R antibody, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:8,

wherein the IFN-γ parameter comprises quantitative information about the level of IFN-γ protein, the level of IFN-γ mRNA, and/or the activity of IFN-γ protein,

wherein the subject has a symptom of multiple sclerosis, and

wherein the IFN-γ parameter of the subject ~~having the excess IFN-γ~~ is decreased at least about ~~2 fold~~ two-fold.

2-4. (Canceled)

5. (Currently amended) The method of claim 1, wherein the IL-21/IL-21R agonist is an agonistic anti-human IL-21R antibody, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:6.

6. (Currently amended) The method of claim 5, wherein the agonistic anti-human IL-21R antibody or ~~the antigen binding~~ antigen-binding fragment thereof is a humanized antibody or ~~an antigen binding~~ antigen-binding fragment thereof.

7. (Original) The method of claim 1, further comprising administering to the subject at least one anti-inflammatory agent.

8. (Previously presented) The method of claim 7, wherein the anti-inflammatory agent is selected from the group consisting of IFNβ-1α and IFNβ-1β.

9. (Currently amended) The method of claim 1, wherein the subject is a human, and the IL-21/IL-21R agonist is a human IL-21 polypeptide that comprises a sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2 and is capable of binding to a human IL-21R.

10. (Original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered in the form of a single dose.

11. (Original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered as a series of doses separated by intervals of days, weeks or months.

12. (Original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered by injection.

13. (Original) The method of claim 12, wherein the IL-21/IL-21R agonist is injected into the central nervous system.

14. (Previously presented) The method of claim 12, wherein the IL-21/IL-21R agonist is injected intrathecally or intravenously.

15. (Original) The method of claim 12, wherein the IL-21/IL-21R agonist is injected into the lumbar cerebrospinal fluid.

16-18. (Canceled)

19. (Previously presented) The method of claim 1, further comprising, after the administering, evaluating the IFN-γ parameter of the subject.

20-28. (Canceled)

29. (Currently amended) A method of decreasing an IFN-γ parameter in a subject having an excess of IFN-γ, the method comprising:

(a) evaluating the IFN-γ parameter of [[a]] the subject;

(b) comparing the IFN-γ parameter [[in]] of the subject to the IFN-γ parameter of a normal subject, wherein a substantial increase in the IFN-γ parameter [[in]] of the subject relative to the normal subject indicates that the subject has ~~the~~ an excess of IFN-γ; and

(c) administering to the subject ~~having the excess IFN-γ~~ an agonistic interleukin-21 (IL-21) polypeptide, wherein the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2 or a murine IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:4,

wherein the IFN-γ parameter comprises quantitative information about the level of IFN-γ protein, the level of IFN-γ mRNA, and/or the activity of IFN-γ protein,

wherein the subject has a symptom of multiple sclerosis, and

wherein the IFN-γ parameter of the subject ~~having the excess IFN-γ~~ is decreased at least about ~~2 fold~~ two-fold.

30. (Currently amended) The method of claim 29, wherein the subject is human[[,]] and the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2.

31. (Previously presented) The method of claim 30 wherein the human IL-21 polypeptide comprises SEQ ID NO:2.

32. (Previously presented) The method of claim 30 wherein the human IL-21 polypeptide is recombinantly produced.

33. (Previously presented) The method of claim 32 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

34. (Currently amended) A method of increasing an IL-10 parameter [[in]] of a subject having an IL-10 deficiency, the method comprising:

(a) evaluating the IL-10 parameter of [[a]] the subject;

(b) comparing the IL-10 parameter [[in]] of the subject to the IL-10 parameter of a normal subject, wherein a substantial decrease in the IL-10 parameter [[in]] of the subject relative to the normal subject indicates that the subject has an IL-10 deficiency; and

(c) administering to the subject ~~having an IL-10 deficiency~~ an agonistic interleukin-21 (IL-21) polypeptide, wherein the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2 or a murine IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:4,

wherein the IL-10 parameter comprises quantitative information about the level of IL-10 protein, the level of IL-10 mRNA, and/or the activity of IL-10 protein,

wherein the subject has a symptom of multiple sclerosis, and

wherein the IL-10 parameter of the subject ~~having the IL-10 deficiency~~ is increased at least about ~~1.2 fold~~ 1.2-fold.

35. (Currently amended) A method of increasing an IL-10 parameter [[in]] of a subject having an IL-10 deficiency, the method comprising:

(a) evaluating the IL-10 parameter ~~in a~~ of the subject;

(b) comparing the IL-10 parameter [[in]] of the subject to the IL-10 parameter [[in]] of a normal subject, wherein a substantial decrease in the IL-10 parameter [[in]] of the subject relative to the normal subject indicates that the subject has an IL-10 deficiency; and

(c) administering to the subject ~~having an IL-10 deficiency~~ an agonist of [[an]] interleukin-21 (IL-21)/IL-21 receptor (IL-21R), wherein the agonist is selected from the group consisting of:

(i) a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2,

(ii) a murine IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:4,

(iii) an agonistic anti-human IL-21R antibody, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:6, and

(iv) an agonistic anti-murine IL-21R antibody, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:8,

wherein the IL-10 parameter comprises quantitative information about the level of IL-10 protein, the level of IL-10 mRNA, and/or the activity of IL-10 protein,

wherein the subject has a symptom of multiple sclerosis, and

wherein the IL-10 parameter of the subject ~~having the IL-10 deficiency~~ is increased at least about ~~1.2 fold~~ 1.2-fold.

36-50 (Canceled)

51. (Previously presented) The method of claim 9 wherein the human IL-21 polypeptide is recombinantly produced.

52. (Previously presented) The method of claim 51 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

53. (Canceled)

54. (Currently amended) The method of claim 34, wherein the subject is human[[,]] and the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2.

55. (Previously presented) The method of claim 54 wherein the human IL-21 polypeptide comprises SEQ ID NO:2.

56. (Previously presented) The method of claim 54 wherein the human IL-21 polypeptide is recombinantly produced.

57. (Previously presented) The method of claim 56 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

58. (Canceled)

59. (Currently amended) The method of claim 35, wherein the subject is a human and the agonist is a human IL-21 polypeptide that comprises a sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:2 and is capable of binding to a human IL-21R.

60. (Previously presented) The method of claim 59 wherein the agonist is a human IL-21 polypeptide that comprises the amino acid sequence of SEQ ID NO:2.

61. (Previously presented) The method of claim 60 wherein the human IL-21 polypeptide is recombinantly produced.

62. (Previously presented) The method of claim 61 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

63. (Currently amended) The method of claim 35, wherein the agonist is an agonistic anti-human IL-21R antibody or an antigen-binding fragment thereof capable of binding to an IL-21R comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO:6.

64. (Previously presented) The method of claim 63, wherein the agonistic anti-human IL-21R antibody or the antigen binding fragment thereof is a humanized antibody or an antigen binding fragment thereof.

65. (Previously presented) The method of claim 35, further comprising administering to the subject at least one anti-inflammatory agent.

66. (Previously presented) The method of claim 65, wherein the anti-inflammatory agent is selected from the group consisting of IFNβ-1α and IFNβ-1β.

67. (Previously presented) The method of claim 35, wherein the IL-21/IL-21R agonist is administered in the form of a single dose.

68. (Previously presented) The method of claim 35, wherein the IL-21/IL-21R agonist is administered as a series of doses separated by intervals of days, weeks or months.

69. (Previously presented) The method of claim 35, wherein the IL-21/IL-21R agonist is administered by injection.

70. (Previously presented) The method of claim 69, wherein the IL-21/IL-21R agonist is injected into the central nervous system.

71. (Previously presented) The method of claim 69, wherein the IL-21/IL-21R agonist is injected intrathecally or intravenously.

72. (Previously presented) The method of claim 69, wherein the IL-21/IL-21R agonist is injected into the lumbar cerebrospinal fluid.

73. (Previously presented) The method of claim 35, further comprising, after the administering, evaluating the IL-10 parameter of the subject.

74. (New) The method of claim 9, wherein the IL-21/IL-21R agonist is a human IL-21 polypeptide that comprises the amino acid sequence of SEQ ID NO:2.